of it implies that menstruation represents the breakdown of the pro-oestrous uterine growth which heralds the succeeding ovulation, combined with (in his own words "tele-scoped into") the breakdown of the pseudo-pregnant endometrial growth which followed the preceding ovulation. This, however, means that the follicular phase, or pro-oestrus, comes to an end at the very beginning of a menstrual cycle, and that an interval of at least ten days elapses between the end of the pro-oestrous destruction and the ovulation which follows. Actually the follicular phase, or pro-oestrus, continues at least throughout the earlier half of the menstrual cycle, as the changes in the sexual skin show.

In spite of the objections to Marshall's hypothesis, the view that the menstrual and oestrous cycles both consist of two phases, but in different combination, seems to my mind the most reasonable explanation of the menstrual cycle, and in the light of facts revealed in the past few years it is possible to state it in a way not open to the criticisms to which Marshall's interpretation is exposed. As I see it,²⁹ the main difference between the menstrual cycle of the primate and the oestrous cycle of the lower mammal lies in the distribution of their respective follicular phases.* In an animal like the bitch, the follicular phase ends with oestrous degeneration, which separates it from the ensuing luteal phase, and the endometrium of pseudo-pregnancy is built up, under the influence of the luteal hormones, from an endometrium that has degenerated at the time of ovulation. In the primate, on the other hand, though the main effects of the oestrous phase occur in the earlier half, they are prolonged over the entire cycle, and in cycles with ovulation, pseudo-pregnant growth is superimposed upon a persisting pro-oestrous endometrium maintained apparently by the follicular hormone. The menstruation which ends such cycles may be taken to represent both pro-oestrous and pseudo-pregnant degeneration.

As I have stated elsewhere,²⁹ if this interpretation is correct, the differences in sexual behaviour between primates and lower mammals largely reflect their different sexual physiological mechanisms. The mating or oestrous phase of the lower mammal is generally brief, whereas that of the primate is diffused over the entire cycle, coinciding with the continuous action of the follicular hormone, but varying in frequency according to the varying degrees of activity of that hormone. In their sexual behaviour, as in many other features, primates thus fail to exhibit an apparent specialization which characterizes all other orders of mammals.

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* Using the term to mean the period in which the follicular hormone (oestrin) functions.

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HEADACHE PRODUCED BY HISTAMINE AND ITS MECHANISM*

BY

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A factor that has always hindered the understanding of headache has been the difficulty of studying it under well-defined circumstances. It seemed to us that a step forward could be made if, by simple means, we could produce headache at will. From its use in other investigations we knew histamine to be suitable for the purpose, and the following is a brief preliminary account of observations made with this substance. We have worked as far as possible on normal subjects, and have always injected the histamine intravenously, thus ensuring the quantity entering the circulation in a given time.

The effects of histamine may be divided into those that are objective, largely vascular, and those that are subjective, of which headache is the most striking, and the only one which concerns us here; these two effects are not simultaneous, the objective changes preceding the subjective. Following an intravenous injection of 0.1 mg. histamine acid phosphate (the dose usually employed by us) nothing happens for an interval during which the substance is travelling to the systemic capillaries. At about the twentieth second a metallic taste is felt in the mouth, and simultaneously the face flushes and systolic and diastolic blood pressures begin to fall. If lumbar puncture has been performed, the cerebro-spinal fluid pressure is found at this time suddenly to rise. This rise in cerebro-spinal fluid pressure has been recently observed by Weiss, Lennox, and Robb,¹ who find it to be accompanied by cerebral vaso-dilatation; for after injecting histamine they observed flushing, bulging, and increased pulsation of a human brain exposed at operation. The changes in facial colour, in arterial blood pressure, and in cerebro-spinal fluid pressure progress for a further period of ten to twenty seconds, and then begin to pass away. The total duration of the facial flush is about three minutes, of the rise in lumbar pressure about one and a half minutes, and of the fall of arterial pressure about thirty seconds.

Headache begins about forty seconds after the onset of vaso-dilatation, when the facial flush is just beginning to fade, when arterial pressure is at its resting level or above, and when lumbar pressure is falling from its peak value. It reaches a maximum about half a minute after its onset, begins to lessen about a minute later, and finally disappears after it has been present for six to ten minutes. The headache is at first conspicuously throbbing in character, waxing and waning with the pulse beat; as time passes, it tends to become continuous, and is not

* A preliminary communication of work done on behalf of the Medical Research Council.

influenced by the pulse during the last three to four minutes of its course. The ache begins in the forehead, and, while remaining most intense there, tends, at its height, to invade the temples, the convexity of the calvarium, and occasionally the occipital region.

Thus the results of injecting histamine intravenously appear to be divisible into two phases. The first is that in which vaso-dilatation begins and progresses to a maximum; this phase is not accompanied by headache. The second phase, that of the decline of vaso-dilatation, is marked by the onset and progressive development of headache, which persists, though lessening, when all objective evidence of vaso-dilatation has disappeared. The beginning of headache appears, therefore, to be related to the decline of vaso-dilatation. That this is not fortuitous is shown by the following observations. While the histamine headache is at its height a second injection of the substance quickly abolishes the headache, which returns about twenty seconds later. A similar transient relief of histamine headache is produced by amyl nitrite. Again, if, instead of making a single injection of histamine, the substance is infused into a vein at a steady rate for long periods, then in the majority of subjects, but not in all, headache does not appear so long as the infusion is continued, but begins about thirty seconds after the infusion is stopped.

From the facts already described we are able to dispose of several possible explanations of the histamine headache. Thus the headache is not due to simple rise of intracranial pressure. This is shown by the lack of coincidence between the rise and fall of lumbar pressure and the onset and disappearance of headache. Moreover, if, when the headache is fully developed, the jugular veins are compressed in the neck, a rise in lumbar pressure occurs, but simultaneously headache is relieved, to return when compression is stopped. The same relief is obtained by artificially raising the intracranial pressure in other ways. It is also clear that headache does not directly result from an expansion of the brain due to dilatation of its vessels, for the headache is absent when this process is at its height, appearing only as vaso-dilatation subsides. The curve of intracranial pressure recorded from a cranial defect follows the same course as does the lumbar pressure curve in response to an injection of histamine, indicating that pressure is raised both above and below the tentorium. Thus on the two sides of the tentorium no pressure difference is established which would tend to stretch this membrane.

There are, however, some indications of where and how the headache arises. That the headache arises in the meninges is suggested by the observation that it is always very greatly increased by a rapid oscillatory movement of the head about either a horizontal or a vertical axis. In such movement, the brain, poised as it is in a bath of cerebro-spinal fluid, must tend to oscillate out of phase with the calvarium, and hence to strain the meninges, which separate it from its rigid case. It has already been pointed out that raising intracranial pressure relieves an established headache; a similar effect is produced by artificially lowering the arterial blood pressure. These facts suggest that the headache arises from stretching of the walls of the cerebral arteries or the tissue in their immediate neighbourhood, for the headache is inhibited either by a rise of pressure outside these vessels or by a fall of pressure within them. Entirely consistent with a simple mechanical effect, such as stretching of a sensitive meningeal structure, are the sudden rise in the intensity of the headache which occurs with the pulse beat, the very quick relief effected by raising the intracranial pressure, and the striking effects of shaking of the head. The outstanding fact for explanation is that while the development of the mechanical stimulus is

related to vaso-dilatation, it long outlasts the objective signs of this process. There seems to be more than one way in which this may be explained. First, the dilator action of histamine on the cerebral arteries may conceivably outlast its action on the minute vessels. If this were so, then the loss of tone of the cerebral arteries might not at first result in their expansion, since this would be prevented by the rise of pressure outside these vessels and the fall of pressure within them; the expansion of the arteries would occur as intracranial and arterial pressures returned to their normal levels. On this hypothesis over-expansion of the cerebral arteries would be the cause of histamine headache. In the second place, cerebral vaso-dilatation may redistribute cerebro-spinal fluid in a manner that is not immediately reversible when vaso-dilatation subsides. This redistribution of fluid might be supposed, if unbalanced by vaso-dilatation, to set up a state of tension in the vascular meninges and thus to produce headache. It is impossible in the present state of knowledge to decide which of these hypotheses, if either, is correct.

The present account of our observations has been made as brief as possible and is in many ways incomplete. It is hoped, however, that enough has been said to show that one variety of headache has quite definite attributes, and that it may be ascribed to a state of tension set up in the meninges. We do not claim, or indeed believe, that all headaches arise in this way; but before this question can be answered it will be necessary to define more closely the attributes of the headaches peculiar to different diseases. Although this work is in progress it is too early to speak of it here.

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THE USE OF A MODIFIED DOUBLE THOMAS FRAME IN THE TREATMENT OF THE PARALYSES OF POLIOMYELITIS

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The epidemics of poliomyelitis which recurred in Victoria each summer and autumn from 1927 to 1931 left behind them annually from eighty to two hundred persons wounded by the lesions of the disease. Paralysis had usually reached its maximum within ten or fourteen days from the onset. It was realized that the future of these patients depended upon two factors:

1. The degree and extent of the initial destruction of the anterior horn cells of the spinal cord, and
2. The perfection of the detail of the care available from the hour of the onset of paralysis.

The teachings of Hugh Owen Thomas, C. Fayette Taylor, and Sir Robert Jones warned us that deformities were not essential sequelae of the disease, but were in every instance preventable, and that the natural tendency towards recovery of function would be handicapped if measures were not taken to protect partially paralysed muscles from the influence of two factors which inevitably operated in uncared for cases, after the disease has done its worst. These are: (a) the functional disability which follows continued stretching of partially paralysed muscles and the development of contractures in muscles favoured by prolonged relaxation, and (b) the influence of fatigue.